



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



## Medical Imagery

## Oral mucosal lesions in a COVID-19 patient: New signs or secondary manifestations?



## ARTICLE INFO

## Article history:

Received 29 May 2020

Received in revised form 3 June 2020

Accepted 4 June 2020

## Keywords:

COVID-19

SARS-CoV-2

Oral conditions

Recurrent herpes simplex

Candidiasis

Geographic tongue

Case report

## ABSTRACT

Some oral manifestations have been observed in patients with coronavirus disease 2019 (COVID-19). However, there is still a question about whether these lesions are due to coronavirus infection or secondary manifestations resulting from the patient's systemic condition. Thus, this article aims to report an additional case of an oral condition in a patient diagnosed with COVID-19. Our patient, a sixty-seven-year-old Caucasian man, tested positive to coronavirus and presented oral manifestations such as recurrent herpes simplex, candidiasis, and geographic tongue. We support the argument that some oral conditions could be secondary to the deterioration of systemic health or due to treatments for COVID-19. The present case report highlights the importance of including dentists in the intensive care unit multi-professional team to improve oral health in critical patients, not only COVID-19 patients, but also, to contribute to evidence-based and decision-making in managing infectious diseases.

© 2020 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

## Introduction

The novel coronavirus disease 2019 (COVID-19) presents an important and urgent threat to global health. The novel coronavirus was initially named 2019-nCoV and officially as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (WHO, 2020). The lungs are the primary site of infection for COVID-19, with patients presenting symptoms ranging from mild flu-like symptoms to fulminant pneumonia and potentially lethal respiratory distress (Guan et al., 2020).

There have been some COVID-19 cases reporting oral manifestations (Chaux-Bodard et al., 2020; de Maria et al., 2020; Lechian et al., 2020; Martín Carreras-Presas et al., 2020; Putra et al., 2020). Since the oral health of COVID-19 patients can be affected by the infection, there is still doubt whether these manifestations could be a typical pattern resulting from the direct viral infection. Perhaps oral lesions may result from systemic deterioration, considering the possibility of opportunistic infections and also adverse reactions to treatments. Therefore, the range of COVID-19 manifestations in the oral cavity has broad and current interest. This brief article's overall objective was to report a relevant case of oral manifestations in a COVID-19 patient.

## Case report

On March 31, 2020, a sixty-seven-year-old Caucasian man with a history of cruising the Brazilian coast in the past 30 days, was admitted at Hospital Alvorada Brasília, Brasília, Brazil. Ten days earlier, the patient developed respiratory symptoms, progressive

dyspnea on exertion, and fever, and diarrhea. The patient was asked about symptoms of gustatory and olfactory dysfunction, and he reported hypogeusia. In the medical history, the patient reported coronary disease, already revascularized, systemic hypertension, autosomal dominant polycystic kidney disease, and kidney transplant, which led him to take immunosuppressants regularly and to use pharmacological prophylaxis for pulmonary venous thromboembolism with Enoxaparin sodium (Clexane<sup>®</sup> 20 mg/day). A nasopharyngeal swab following reverse-transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2 RNA amplification tested positive. Chest computed tomography evidenced bilateral diffuse hyperdense infiltrations in the so-called “ground glass” pattern affecting both lungs, leading to intensive care unit (ICU) admission for supplemental O<sub>2</sub>. After that, the patient underwent orotracheal intubation due to disease progression and respiratory failure, and the patient was treated with Hydroxychloroquine sulfate (Reuquinol<sup>®</sup>, 400 mg/day), Ceftriaxone sodium (2 g/day), and Azithromycin (Zitromax<sup>®</sup> 500 mg/day) for seven days.

Due to clinical suspicion of pneumonia associated with mechanical ventilation, and worsening of the white blood cell count, a new antibiotic regimen was started with Meropenem (Meropenem<sup>®</sup>, 1000 mg, 8/8 hs) and Sulfamethoxazole + Trimetoprim (Bactrim<sup>®</sup>, 400 mg + 80 mg, 1.5 ampule, 8/8 hs) for ten days. Then, the patient underwent a tracheostomy. Hemodialysis was performed with subsequent recovery of renal function. Mechanical ventilation was maintained with good recovery and the possibility of spontaneous breathing. The patient also returned to the use of immunosuppressants and pharmacological prophylaxis for venous

<https://doi.org/10.1016/j.ijid.2020.06.012>

1201-9712/© 2020 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

and pulmonary thromboembolism with Enoxaparin sodium (Clexane<sup>®</sup> 60 mg/day).

On the twenty-fourth day of hospitalization, the dentists (RLC S and RMP) were called to assess a persistent white plaque on the tongue dorsum. This lesion was previously treated by physicians with intravenous Fluconazole (Zoltec<sup>®</sup> 200 mg/100 mL, one bag a day for ten days) and oral nystatin (100,000 IU/mL, 8/8 h, for 30 days), but no regression was observed. In addition to the white plaque, the dentist also observed multiple pinpoint yellowish ulcers on the tongue dorsum resembling the late stage of herpetic recurrent oral lesions (Figure 1A). After a complete intraoral examination, no other lesions on the oral mucosa were observed, except for a nodule located in the lower lip, measuring approximately 1 cm in its largest diameter, suggestive of a reactive lesion (fibroma) that was confirmed by the patient's pre-existing conditions. Tongue scrape culture was performed, which was compatible with *Saccharomyces cerevisiae*. Extremely viscous saliva was observed; biopsies were not recommended due to the patient's systemic conditions. And, cutaneous lesions were not observed during the patient's physical examination. At this time, the patient kept the antifungals and was treated with chlorhexidine digluconate (0.12%) alcohol-free mouth rinses, and daily applications of 1% hydrogen peroxide. The dentist also instructed

the health team on the importance of maintaining oral hygiene care.

Two weeks after the first oral examination, the white lesions on the tongue dorsum showed almost complete resolution. In a new intraoral examination, it was observed that the patient presented an asymptomatic geographic tongue classified as severe, according to the severity index recently published (Picciani et al., 2020) (Figure 1B), associated with fissured tongue.

The patient was discharged from the ICU, and in subsequent days, there was a prompt recovery. The patient had no fever, and the physician was able to gradually decrease oxygen flow, discontinuing antibiotic therapies. At that moment, in a hospital apartment, he was conscious, oriented, and not dependent on oxygen therapy. Also, the patient had no complaints, preserved appetite, good water consumption, good urine volume, and was afebrile.

On May 14, the patient was discharged after forty-four days of hospitalization; the dentist only prescribed oral health care. Ten days later, the patient sent us an intraoral image in which maintenance of geographic tongue could be observed, but it was now classified as moderate, according to the severity index recently published (Picciani et al., 2020). Also, a slightly erythematous area could be seen in the right palatine tonsil



**Figure 1.** (A) April 24, 2020. COVID-19 patient presenting a white plaque on the tongue dorsum, centrally located, associated with several small, circle-shaped yellowish ulcers resembling the late stage of herpetic recurrent oral lesions associated with candidiasis. A nodule located in the lower lip was observed, measuring approximately 1 cm in its largest diameter, suggesting a reactive lesion (fibroma). (B) May 7, 2020. COVID-19 patient presenting atrophic areas surrounded by an elevated yellow-white halo classified as severe geographic tongue according to the severity index scoring system (Picciani et al., 2019) associated with fissured tongue. Also, the tongue's white lesions, suggestive of candidiasis, showed almost complete resolution. (C) May 25, 2020. The patient, recovered from COVID-19, showing atrophic areas surrounded by an elevated yellow-white halo classified as moderate geographic tongue according to the severity index scoring system (Picciani et al., 2020). We could observe a slightly erythematous area in the right palatine tonsil region; however, the patient reported being asymptomatic.

region; however, the patient reported being asymptomatic (Figure 1C).

## Discussion

Current research shows that coronavirus damage to respiratory and other organs could be related to the distribution of angiotensin-converting enzyme 2 (ACE2) receptors in the human system (Zou et al., 2020). Therefore, cells with ACE2 receptor distribution may become host cells for the virus and further cause inflammatory reactions in related organs and tissues, such as the tongue mucosa and salivary glands (Xu et al., 2020). Besides, available evidence has not established an efficient and safe pharmacological agent against COVID-19 yet, and the potential ones are related to several adverse reactions, including oral lesions (Godinho et al., 2020; Mehra et al., 2020; de Melo Filho et al., 2012; National Center for Biotechnology Information, 2020). Also, COVID-19 acute infection, along with associated therapeutic measures, could potentially contribute to adverse outcomes concerning oral health, likely leading to various opportunistic fungal infections, recurrent oral herpes simplex virus (HSV-1) infection, unspecific oral ulcerations, fixed drug eruptions, dysgeusia, xerostomia linked to decreased salivary flow, ulcerations and gingivitis as a result of the impaired immune system and/or susceptible oral mucosa (Dziedzic and Wojtyczka, 2020).

The oral conditions presented by our patient and other cases already reported (Martín Carreras-Presas et al., 2020; Putra et al., 2020) supports the hypothesis that they are highly suggestive of secondary lesions resulting from the deterioration of systemic health or due to treatments for COVID-19. Even considering our interpretation of associated conditions, the dentist's relevance as part of the multi-disciplinary team in supporting critical patients in ICU, such as COVID-19, should be highlighted. Also, dental follow up after the patient is dismissed from the hospital must be provided. In COVID-19 patients we should consider the occurrence of some oral signs and symptoms, including dysgeusia, petechiae, candidiasis, traumatic ulcers, HSV-1 infection, geographical tongue, thrush-like ulcers, among others. Thus, the importance of the clinical dental examination of patients with infectious diseases in the ICU should be emphasized, considering the need for support, pain control, and quality of life.

## Author contributions

ENSG, JAS, and AGCN: Conceptualization, study design, literature research, writing-original draft. RLCS, RMP, and ACC: Clinical studies, treating the patient, data acquisition, writing-review. ARSS: Validation, writing-review.

## Ethical approval and informed consent

The study has been conducted in full accordance with ethical principles (Declaration of Helsinki), and written informed consent was obtained from the patient.

## Funding

Decanato de Pesquisa e Inovação, Universidade de Brasília, EDITAL DPI-UnB No 04/2019 – (ENSG grant 33902001).

## Conflicts of interest

None to declare.

## References

- Chaux-Bodard A-G, Deneuve S, Desoutter A. Oral manifestation of Covid-19 as an inaugural symptom?. *J Oral Med Oral Surg* 2020;26:18.
- de Maria A, Varese P, Dentone C, Barisione E, Bassetti M. High prevalence of olfactory and taste disorder during SARS-CoV-2 infection in outpatients. *J Med Virol* 2020;(May), doi:http://dx.doi.org/10.1002/jmv.25995.
- de Melo Filho MR, da Silva CA, da Rocha Dourado M, de Oliveira Pires MB, Pêgo SP, de Freitas EM. Palate hyperpigmentation caused by prolonged use of the anti-malarial chloroquine. *Head Neck Pathol* 2012;6(1):48–50, doi:http://dx.doi.org/10.1007/s12105-011-0288-5.
- Dziedzic A, Wojtyczka R. The impact of coronavirus infectious disease 19 (COVID-19) on oral health. *Oral Dis* 2020;, doi:http://dx.doi.org/10.1111/odi.13359 Accepted author manuscript.
- Godinho GV, Paz ALLM, de Araújo Gomes EPA, Garcia CL, Volpato LER. Extensive hard palate hyperpigmentation associated with chloroquine use. *Br J Clin Pharmacol* 2020;, doi:http://dx.doi.org/10.1111/bcp.14313.
- Guan W, Ni Z, Hu Y, Liang W, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020;382:1708–20, doi:http://dx.doi.org/10.1056/NEJMoa2002032.
- Lechien JR, Chiesa-Estomba CM, De Siaty DR, Horoi M, Le Bon SD, Rodriguez A, et al. Olfactory and gustatory dysfunctions as a clinical presentation of mild-to-moderate forms of the coronavirus disease (COVID-19): a multicenter European study. *Eur Arch Otorhinolaryngol* 2020;1–11, doi:http://dx.doi.org/10.1007/s00405-020-05965-1.
- Martín Carreras-Presas C, Amaro Sánchez J, López-Sánchez AF, Jané-Salas E, Somacarrera Pérez ML. Oral vesiculobullous lesions associated with SARS-CoV-2 infection. *Oral Dis* 2020;(May), doi:http://dx.doi.org/10.1111/odi.13382.
- Mehra MR, Desai SS, Ruschitzka F, Patel AN. Hydroxychloroquine or chloroquine with or without a macrolide for treatment of COVID-19: a multinational registry analysis. *Lancet* 2020;, doi:http://dx.doi.org/10.1016/S0140-6736(20)31180-6 Published online May 22, 2020.
- National Center for Biotechnology Information. PubChem Database. Ritonavir, CID=392622. 2020. <https://pubchem.ncbi.nlm.nih.gov/compound/Ritonavir>.
- Picciani BLS, Santos LR, Teixeira-Souza T, Dick TNA, Carneiro S, Pinto JMN, et al. Geographic tongue severity index: a new and clinical scoring system. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2020;129(4):330–8, doi:http://dx.doi.org/10.1016/j.oooo.2019.12.007.
- Putra BE, Adiarto S, Dewayanti SR, Juzar DA. Viral exanthem with “pin and needles sensation” on extremities of COVID-19 patient. *Int J Infect Dis* 2020;(May), doi: http://dx.doi.org/10.1016/j.ijid.2020.05.020 pii: S1201-9712(20)30327-1.
- World Health Organization. Novel coronavirus(2019-nCoV) situation report – 22 – data as reported by February 11, 2020. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1\\_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200211-sitrep-22-ncov.pdf?sfvrsn=fb6d49b1_2).
- Xu H, Zhong L, Deng J, Peng J, Dan H H, Zeng X, et al. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. *Int J Oral Sci* 2020;12(8), doi:http://dx.doi.org/10.1038/s41368-020-0074-x.
- Zou X, Chen K, Zou J, Han P, Hao J, Han Z. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. *Front Med* 2020;14(2):185–92, doi:http://dx.doi.org/10.1007/s11684-020-0754-0.

Juliana Amorim dos Santos<sup>a</sup>

Ana Gabriela Costa Normando<sup>a,b</sup>

Rainier Luiz Carvalho da Silva<sup>a,c</sup>

Renata Monteiro De Paula<sup>c</sup>

Allan Christian Cembranel<sup>c</sup>

Alan Roger Santos-Silva<sup>b</sup>

Eliete Neves Silva Guerra<sup>a,\*</sup>

<sup>a</sup>Laboratory of Oral Histopathology, Health Sciences Faculty, University of Brasília (UnB), Brasília, Brazil

<sup>b</sup>Oral Diagnosis, Piracicaba Dental School, University of Campinas (UNICAMP), São Paulo, Brazil

<sup>c</sup>Hospital Alvorada Brasília, Brasília, Federal District, Brazil

\* Corresponding author at: Health Sciences Faculty, University of Brasília, Asa Norte, Brasília, DF, 70910-900, Brazil.  
E-mail address: elieteneves@unb.br (E. Guerra).

Received 29 May 2020

Received in revised form 3 June 2020

Accepted 4 June 2020